UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,181	09/21/2005	Shailesh Bhamare	11336.1004USWO	1149

52835 7590 05/22/2008

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. BOX 2902
MINNEAPOLIS, MN 55402-0902

EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
05/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,181	BHAMARE ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-8) in the reply filed on March 7, 2008 is acknowledged.

The traversal is on the ground(s) that US 2002/0039594 ('594) teaches solid porous matrix comprising a surfactant in combination with a therapeutic and that the reference does not direct one of ordinary skill to the specific combination of the present invention. This is not found persuasive because instant claim one recites "the composition comprising" which is open language and does not exclude the presence of additional ingredients.

Applicant traverses that the mere disclosure that the system of '594 may contain ACE inhibitor or meglumine antimonite (and not meglumine alone which is distinct from the salt) cannot render obvious the present invention, which achieves a stabilized composition of ACE inhibitor with the presence of meglumine as a stabilizer. This is not found persuasive because one with ordinary skill in the art would find it obvious to combine the disclosed ACE inhibitor and the meglumine antimonite and would use meglumine or meglumine salts in the composition during the process of routine experimentation.

The restriction requirement is still deemed proper and is therefore made FINAL.

2. Claims 19-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

3. Claim 23 was cancelled.

4. Claims 1-18 are included in the prosecution.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 9/21/05 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement.

See attached copy of PTO-1449.

Claim Objections

6. Claim 15 is objected to because of the following informalities: Line 2 of claim 15 recites "atleast" which should be corrected to "at least". Appropriate correction is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garg et al. (WO 03/063825) in view of Fülbreth et al. (US 5,151,433).

The claimed invention is a stabilized pharmaceutical solid composition comprising an ACE inhibitor and meglumine.

Garg teaches meglumine as an alkalinizing agent (Page 11, lines 1-3) and a therapeutically active moiety including the ACE inhibitor captropil (Page 10, lines 17-18) in a solid tablet formulation (Abstract).

Garg does not expressly teach ramipril as the ACE inhibitor.

Fülbreth teaches ACE inhibitors that are administered orally and solid formulations such as tablets or capsules (Col. 1, lines 40-42 and lines 53-56). Fülbreth teaches ramipril tablets stabilized against mechanical stress (Col. 4, lines 1-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid tablet composition with meglumine and an ACE inhibitor, as suggested by Garg, use ramipril as the ACE inhibitor in the tablet formulation, as taught by Fülbreth, and produce the instant invention.

One of ordinary skill in the art would to do this because both Garg and Fülbreth teach solid tablet formulations with ACE inhibitors and it would be obvious to try an alternative ACE inhibitor, such as the ramipril taught by Fülbreth in the tablet of Garg during the process of routine experimentation. Furthermore, Fülbreth teaches ramipril tablets stabilized against mechanical stress (Col. 4, lines 1-15).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of a stabilized solid composition would have been obvious over the stable tablet formulations taught by Garg. "The formulations can be expected to have a reasonable shelf life as shown by the accelerated stability data for 3 months, which demonstrates that the release profile is similar to that of initial samples" (Page 23, lines 12-14). The limitation of an ACE inhibitor would have been obvious over the ACE inhibitor captropil taught by Garg (Page 10, lines 17-18). The limitation of meglumine would have been obvious over the meglumine taught by Garg (Page 11, lines 1-3).

Regarding instant claims 2-3, the limitation of ramipril would have been obvious over the ramipril taught by Fülbreth (Col. 4, lines 1-15).

Regarding instant claim 4, the limitation of 1mg to about 10mg ramipril in the composition would have been obvious over the 2.5mg ramipril tablets taught by Fülbreth (Col. 6, Table 1).

Regarding instant claims 5-6, the limitation of the ratio of ACE inhibitor to meglumine would have been obvious over the ratio of the therapeutically active ingredient (such as captopril) to the alkalinizing agent (meglumine) that is in the range of 0.1:9.9 to 7:3 (Page 11, lines 7-8) in view of the ramipril tablets taught by Fülbreth (Col. 6, Table 1). One with ordinary skill in the art would modify the ratio of the ACE inhibitor to the meglumine during the process of routine experimentation in order to achieve the desired dosage and stability criteria because this is a manipulatable parameter.

9. Claims 7-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garg et al. (WO 03/063825) in view of Fülbreth et al. (US 5,151,433) and further in view of Avrutov et al. (US 2002/0022646).

The teachings of Garg and Fülbreth with respect to the ACE inhibitor and meglumine are stated above.

Garg and Fülbreth do not expressly teach low substituted hydroxypropyl cellulose and pregelatinized starch.

Avrutov teaches tablet excipients including pregelatinized starch, low substituted hydroxypropyl cellulose and tableting lubricants like magnesium and calcium stearate (Page 4, [0038]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid tablet composition with meglumine and an ACE inhibitor, as suggested by Garg, use ramipril as the ACE inhibitor in the tablet formulation, as taught by Fülbreth, further use the low substituted hydroxypropyl cellulose and pregelatinized starch in the tablet formulation, as taught by Avrutov, and produce the instant invention.

One of ordinary skill in the art would to do this because the diluents low substituted hydroxypropyl cellulose and pregelatinized starch are known to be used in tablets, as evidenced by Avrutov. It would be obvious to use the commonly used diluents in the tablet formulations taught by Garg and Fülbreth.

Regarding instant claims 7-8, the diluents low substituted hydroxypropyl cellulose and pregelatinized starch would have been obvious over the pregelatinized starch and low substituted hydroxypropyl cellulose used as tableting excipients by Avrutov (Page 4, [0038]).

Regarding instant claim 9, the limitation of the ratio of ACE inhibitor to diluent would have been obvious over the pregelatinized starch and low substituted hydroxypropyl cellulose used as tableting excipients by Avrutov (Page 4, [0038]). One with ordinary skill in the art would find it obvious to modify the ratio of ACE inhibitor to diluent during the process of routine experimentation in order to optimize the tablet dosage and stability. The recited ratio would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claims 10-12, the limitation of the composition further comprising a lubricant would have been obvious over the magnesium stearate taught by Garg (Page 29, line 1) and by the magnesium and calcium stearate taught by Avrutov (Page 4, [0038]).

Regarding instant claims 13-14, the limitation of the amount of lubricant in the composition would have been obvious over the lubricant in the tablets taught by Garg (Page 29, line 1) and Avrutov (Page 4, [0038]) because one with ordinary skill in the art would modify the level of the lubricant in the formulation during the process of routine experimentation and the recited range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 15, the stabilized pharmaceutical ACE inhibitor composition would have been obvious over the tablet with an ACE inhibitor and meglumine as taught by Garg (Page 11, lines 1-3, Page 10, lines 17-18 and Abstract) in view of the ramipril tablets stabilized against mechanical stress as taught by Fülbreth (Col. 4, lines 1-15). The limitation of meglumine would have been obvious over the meglumine taught by Garg (Page 11, lines 1-3). The limitation of low substituted hydroxypropyl cellulose and pregelatinized starch would have been obvious over the pregelatinized starch and low substituted hydroxypropyl cellulose used as tableting excipients by Avrutov (Page 4, [0038]). The limitation of magnesium stearate would have been obvious over the magnesium stearate taught by Garg (Page 29, line 1) and by the magnesium stearate taught by Avrutov (Page 4, [0038]).

Regarding instant claims 16-18, the dosage form, capsule and tablet would have been obvious over the granules that are used to manufacture capsules or tablets (Col. 6, lines 21-23).

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615